

Appln. No.: 09/373,230
Amdt. dated: December 1, 2005
Reply to Office Action of June 3, 2005

Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

Claims 1 and 2 (Cancelled).

3 (Currently amended). A purified interferon-gamma (IFN- γ) production inducing protein, which is a variant of an interferon-gamma (IFN- γ) production inducing protein, also known as IGIF and IL-18, and which has the following physicochemical properties:

- (1) Molecular weight
19,000 \pm 5,000 daltons on gel filtration and sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE);
- (2) Isoelectric point (pI)
4.8 \pm 1.0 on chromatofocusing;
- (3) Biological activity
Inducing the interferon- γ production by immunocompetent cells, and activating the cytotoxicity of killer cells, where the activation is augmented by interleukin 2; [[and]]
- (4) Partial amino acid sequence

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Possessing a part or the whole of the amino acid sequence of SEQ ID NO:2, wherein the Xaa in SEQ ID NO:2 is Met or Thr,

(5) Purity

Exhibiting a single protein band when electrophoresed on sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE); and

(6) Assay

Being detected with a monoclonal antibody which binds to the interferon- γ inducing polypeptide having an amino acid sequence of SEQ ID NO:2,

wherein said variant ~~is a sequence variant of SEQ ID NO:2 which corresponds to the~~ has an amino acid sequence which is at least 90% homologous to, but different from the amino acid sequence of SEQ ID NO:2, ~~which is obtainable by replacing at least one amino acid residue in SEQ ID NO:2 with a different amino acid residue or by deleting or adding at least one amino acid residue in SEQ ID NO:2 or to the N terminus of SEQ ID NO:2 while not substantially altering~~ while substantially having the above biological activity (3).

4 (Previously presented). The purified protein according to claim 3, wherein said variant has at least one amino

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acid residue in SEQ ID NO:2 replaced with a different amino acid residue.

5(Previously presented). The purified protein according to claim 3, wherein said variant has at least one amino acid residue deleted or added to the N-terminus of SEQ ID NO:2.

6(Previously presented). A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and, as an active ingredient, the protein of claim 3.

7(Previously presented). A purified interferon-gamma (IFN- γ) production inducing protein, also known as IGIF and IL-18, which has the amino acid sequence of SEQ ID NO:2, where Xaa represents methionine or threonine.

8(Previously presented). An interferon-gamma (IFN- γ) production inducing agent which consists essentially of, as an effective ingredient, the protein of claim 7.

9(Original). A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and, as an active ingredient, the protein of claim 7.

Claim 10 (Cancelled)

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11(Currently amended). A purified interferon-gamma (IFN- γ) production inducing protein, also known as IGIF and IL-18, which has the following physicochemical properties:

- (1) Molecular weight
19,000 \pm 5,000 daltons on gel filtration and sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE);
- (2) Isoelectric point (pI)
4.8 \pm 1.0 on chromatofocusing;
- (3) Biological activity
Inducing the interferon- γ production by immunocompetent cells, and activating the cytotoxicity of killer cells, where the activation of cytotoxicity of killer cells being augmented by interleukin-2; [[and]]
- (4) Partial amino acid sequence
Possessing a part or the whole of the amino acid sequence of SEQ ID NO:2, wherein the Xaa in SEQ ID NO:2 is Met or Thr,
- (5) Purity
Exhibiting a single protein band when electrophoresed on sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE); and

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(6) Assay

Being detected with a monoclonal antibody which binds to the interferon- γ inducing polypeptide having an amino acid sequence of SEQ ID NO:2, and which reacts with a monoclonal antibody specific to an interferon-gamma (IFN- γ) production inducing protein having the amino acid sequence of SEQ ID NO:2 or a sequence variant of the protein having an amino acid sequence which is at least 90% homologous to, but different from the amino acid sequence of SEQ ID NO:2, while substantially having one or more of the antigenic fragments of the amino acid sequence of SEQ ID NO:2 while not substantially altering the above biological activity (3).

Claims 12 and 13 (Cancelled)

14 (Currently amended). A purified interferon-gamma (IFN- γ) production inducing protein capable of inducing interferon-gamma (IFN- γ) production by immunocompetent cells, wherein said protein is encoded by a DNA sequence which hybridizes to an oligonucleotide probe of SEQ ID NO:5 under the hybridization conditions of 5 x SSPE, 5 x Denhardt's solution, 0.5 w/v% SDS, 100 μ g/ml denatured salmon sperm DNA, and 45°C and after being washed with 6 x SSC and said protein has the following physicochemical properties:

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(1) Molecular weight

19,000±5,000 daltons on gel filtration and sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE);

(2) Isoelectric point (pI)

4.8 ± 1.0 on chromatofocusing;

(3) Biological activity

Inducing the interferon- γ production by immunocompetent cells, and activating the cytotoxicity of killer cells, where the activation is augmented by interleukin 2; [[and]]

(4) Partial amino acid sequence

Possessing a part or the whole of the amino acid sequence of SEQ ID NO:2, wherein the Xaa in SEQ ID NO:2 is Met or Thr,

(5) Purity

Exhibiting a single protein band when electrophoresed on sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE); and

(6) Assay

Being detected with a monoclonal antibody which binds to the interferon- γ inducing polypeptide having an amino acid sequence of SEQ ID NO:2,

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wherein said protein has an amino acid sequence which is at least 90% homologous to, but different from the amino acid sequence of SEQ ID NO:2, while substantially having the above biological activity (3).

15 (Cancelled) .

16 (Currently amended). An isolated interferon-gamma (IFN- γ) production inducing protein, also known as IGIF and IL-18, which substantially retains its interferon-gamma (IFN- γ) production inducing activity even after treatment with SDS-PAGE, said protein having the following physicochemical properties:

(1) Molecular weight

19,000 \pm 5,000 daltons on gel filtration and sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE);

(2) Isoelectric point (pI)

4.8 \pm 1.0 on chromatofocusing;

(3) Biological activity

Inducing the interferon- γ production by immunocompetent cells, and activating the cytotoxicity of killer cells, where the activation is augmented by interleukin 2; [[and]]

(4) Partial amino acid sequence

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Possessing a part or the whole of the amino acid
sequence of SEQ ID NO:2, wherein the Xaa in SEQ ID
NO:2 is Met or Thr,

(5) Purity

Exhibiting a single protein band when
electrophoresed on sodium dodecylsulfate
polyacrylamide gel electrophoresis (SDS-PAGE); and

(6) Assay

Being detected with a monoclonal antibody which
binds to the interferon- γ inducing polypeptide
having an amino acid sequence of SEQ ID NO:2,
wherein said protein has an amino acid sequence which is at least
90% homologous to, but different from the amino acid sequence of
SEQ ID NO:2, while substantially having the above biological
activity (3).

17(Cancelled).